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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 01/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/655,762	CANTOR ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☒ Claim(s) *4 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 January 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/9/04 & 9/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Remark

The instant application contains misnumbered claims. The second instances of claims 6 and 7 (appearing on page 20 of the application) have been renumbered to claim 8 and 9, respectively, pursuant to 37 C.F.R. 1.126.

With regard to the recitation of erroneous filing year of U.S. Provisional application no. 60/422,030, in the preliminary amendment received on October 29, 2003, the Office acknowledges the typographical error as the ADS correctly identifies the filing year of said provisional application.

Thus, the amendment to the specification made in the Amendment received on February 9, 2004 does not constitute new matter.

Drawings

The drawings are objected to under 37 CFR 1.83(a) because they fail to show the sequence of the competing sequence in Figure 1. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be

labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Information Disclosure Statement

The IDS received on February 9, 2004 and September 30, 2004 are acknowledged.

Signed copies of their PTO-1449 are enclosed herewith.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for reciting the phrase, "a standard nucleic acid having a nucleotide sequence at least one base different than the target." The claim when read as a whole which later recites the phrase, "thereby creating a site of difference between the target and the standard nucleic acid" becomes indefinite because the standard nucleic acid is not limited to having a single nucleotide difference, but reads on a nucleic acid which is completely different in its sequence to that of the target nucleic acids ("at least one"). Hence, it becomes indefinite where the site of difference would be with respect to this embodiment. Clarification is requested.

Claim 1 is indefinite for reciting the phrase, "enhancing the difference" because the difference is in the sequence. Hence, it is unclear how the difference in the nucleotide sequence could be "enhanced."

Claim 1 is indefinite for reciting the phrase, "the enhanced product" because there is insufficient antecedent basis; and second, it is unclear in what aspect the product is "enhanced."

Claims 1-8 and 9 are indefinite by way of their dependency on claim 1.

Claim 6 is indefinite for reciting the term, "allele specific enzyme cleavage," because it is not known that an enzyme which is specific for an allele exists. Clarification is requested.

Claim 8 is indefinite by way of its dependency on claim 6.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 5, 7, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Bunn et al. (U.S. Patent No. 5,213,961, issued May 25, 1993).

Bunn et al. disclose a method of quantifying the amount of a target nucleic acid sequence in a biological sample (column 3, lines 24-26; column 3, lines 46-48), wherein said method comprises the steps of:

a) preparing a sample by adding a known amount of a standard nucleic acid (column 5, lines 25-27, 33, and 34), having a nucleotide sequence at least one base different than the target nucleic

acid sequence (column 5, line 67 to column 6, line 20, specifically line 17-18), which creates a site of differentiation between the target and the standard nucleic acid;

b) amplifying the sample of step a) (column 6, lines 38-40);

c) enhancing the differences between the standard and the target nucleic acid sequence at the site of differentiation (column 6, lines 58-61); and

d) quantifying the enhanced products by measuring the ratio of the amplified target nucleic acid to the amplified standard nucleic acid to measure the amount of target nucleic acid sequence present in the biological sample (column 8, lines 39-45), thereby clearly anticipating claim 1.

With regard to claim 3, the artisans recite that the target nucleic acid could be an mRNA transcript (column 8, lines 52-54).

With regard to claims 5 and 7, the amplification of the target nucleic acid and the standard nucleic acid would result in an increased products which differ in their sequences, and therefore, arguably, enhances the differences. In other words, amplification and enhancing is achieved in a single step. The hybridization of the primers occur in both of the nucleic acid samples, and since the specification does not clearly define what is considered to be "a site of differentiation," the limitation would also be anticipated.

With regard to claim 6, the standard nucleic acid, after amplification, is cleaved with a restriction enzyme, wherein the standard nucleic acid contains a sequence different from that of the target, said difference resulting in a restriction enzyme recognition site (column 6, lines 17-21).

With regard to claim 9, the standard nucleic acid of Bunn et al., which is structurally identical to that of the instant claim, is disclosed as being in a tube (column 10, lines 44 and 50).

Therefore, the invention as claimed is clearly anticipated by Bunn et al.

Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by Arnold et al. (WO 00/50869, published August 31, 2000).

Preliminarily, for the purpose of prior art, claim 7 is drawn to a kit comprising at least one nucleic acid which has at least one nucleotide difference when compared to a target nucleic acid. A kit is defined by the physical element (i.e., reagents) comprised therein. While a printed matter is a physical element, the contents (the actual instruction) therein are not given patentable weight as they only give intended use of the elements of the kit. So long as a disclosure discloses the elements claimed by the instant claim, said disclosure is prior art.

In *In re Ngai*, 70 USPQ 2d 1862 (CAFC 2004) the court, referencing *In re Gulak*, 703 F.2d 1381 (Fed. Cirl. 1983), held that addition of a new set of instructions into a known kit does ***not*** interrelate with the kit in the same way as the numbers interrelate with the kit in the same way as the numbers interrelated with the band (as in *Gulak*). The court held that the printed matter in no way depends on the kit, and the kit does not depend on the printed matter expressing that if a patent were to be granted solely on the presence of a different printed instructions, "anyone could continue patenting a product indefinitely provided that they add a new instruction sheet to the product," concluding that a known product by simply attaching a set of instructions to that product would not be entitled a new patent.

Arnold et al. disclose an isolated nucleic acid sequence comprising a single nucleotide polymorphism. As the nucleic acid comprises at least one nucleotide different than that of the wild type nucleic acid (page 6, lines 3-10), said nucleic acid would be structurally identical to the standard nucleic acid of instant claim.

With regard to the kit, the artisans contemplate a kit comprising reagents and mixtures for their method (page 3, lines 10-12), thereby clearly anticipating claim 7.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bunn et al. (U.S. Patent No. 5,213,961, issued May 25, 1993) in view of Carroll et al. (U.S. Patent No. 5,906,744, issued May 25, 1999).

Bunn et al. disclose a method of quantifying the amount of a target nucleic acid sequence in a biological sample (column 3, lines 24-26; column 3, lines 46-48), wherein said method comprises the steps of:

a) preparing a sample by adding a known amount of a standard nucleic acid (column 5, lines 25-27, 33, and 34), having a nucleotide sequence at least one base different than the target nucleic acid sequence (column 5, line 67 to column 6, line 20, specifically line 17-18), which creates a site of differentiation between the target and the standard nucleic acid;

b) amplifying the sample of step a) (column 6, lines 38-40);

c) enhancing the differences between the standard and the target nucleic acid sequence at the site of differentiation (column 6, lines 58-61); and

d) quantifying the enhanced products by measuring the ratio of the amplified target nucleic acid to the amplified standard nucleic acid to measure the amount of target nucleic acid sequence present in the biological sample (column 8, lines 39-45), thereby clearly anticipating claim 1.

The artisans recite that the target nucleic acid could be an mRNA transcript (column 8, lines 52-54).

The amplification of the target nucleic acid and the standard nucleic acid would result in an increased products which differ in their sequences, and therefore, arguably, enhances the differences. In other words, amplification and enhancing is achieved in a single step.

The standard nucleic acid, after amplification, is cleaved with a restriction enzyme, wherein the standard nucleic acid contains a sequence different from that of the target, said difference resulting in a restriction enzyme recognition site (column 6, lines 17-21).

The standard nucleic acid of Bunn et al., which is structurally identical to that of the instant application, is disclosed as being in a tube (column 10, lines 44 and 50).

Bunn et al. do not explicitly teach that a target nucleic acid from an infectious agent should be employed in their method (claim 2).

Carroll et al. disclose that amplification techniques such as PCR, branched DNA, and nucleic acid sequence based amplification (NASBA) is employed commonly in the art to detect the levels of infectious agents in samples (column 1, lines 23-29, lines 55-56).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to apply the amplification method of Bunn et al. and apply it for quantifying levels of infectious agents in samples, as the desire to do so have been long felt and well-established in the art (diagnosis and prognosis of infectious diseases). Thus, one of ordinary skill in the art would have been motivated to employ the method of Bunn et al. so as to determine the level of infectious agent in a sample. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation success at combining the teachings, for any known quantification method via amplification, as clearly expressed by Carroll et al., would have sufficed.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Double Patenting

Applicant is advised that should claim 4 be found allowable, claim 8 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. Claim 8 is a multiple dependent claim, dependent on at least claim 1. In this embodiment, both claims result in same embodiment of quantifying via MALDI-TOF mass spectrometry. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

No claims are allowed.

Claims 4 and 8 are objected to for being dependent on a rejected base claim.

Applicants are advised that amending the independent claim 1 reflect the specific embodiment disclosed in Figure 1 would appear to render the claims free of prior art.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m. The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (571) 272-0784. If the attempts

to reach the above Examiners are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Young J. Kim
Patent Examiner
Art Unit 1637
1/9/2006

YOUNG J. KIM
PATENT EXAMINER

yjk